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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/522,215	04/07/2005	Elias Castanas	65321(54558)	1523

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EXAMINER	
LUKTON, DAVID	

ART UNIT	PAPER NUMBER
1654	

DATE MAILED: 11/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/522,215	CASTANAS, ELIAS	
	Examiner	Art Unit	
	David Lukton	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28-59* is/are pending in the application.

4a) Of the above claim(s) *34,38-40,42 and 54* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28-33,35-37,41,43-53 and 55-59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Pursuant to the directives of the response filed 8/29/06, claims 28, 29, 44 have been amended, and claims 48-59 added. Claims 28-59 were pending at that point. Pursuant to a supplemental response filed 10/12/06, claim 48 was amended; claims 28-59 remain pending.

Applicants election of Group 9 (claims 28-37, 40, 41, 43, drawn to a method wherein an antiandrogen is not used) is acknowledged. As previously acknowlwedged, the elected disease (to be treated) is prostate cancer. In addition, the elected conjugate is testosterone-3-(O-carboxymethyl oxime/HSA). Given that no "detectable label" has been identified, it is apparent that the elected conjugate is not detectably labeled.

Applicants' arguments filed 10/12/06 have been considered and found persuasive in part. The previously imposed prior art rejection is withdrawn.

Claims 28-33, 35-37, 41, 43-53, 55-59 are examined in this Office action; claims 34, 38-40, 42, 54 are withdrawn from consideration.

✧

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it in such full, clear, concise and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 28-33, 35-37, 41, 43-53, 55-59 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are drawn to a method of treating any proliferative disorder that could be characterized as a "solid cancer" or "haematological malignancy". These two classes of disease encompass a variety of medical conditions; many of the following are included:

> breast cancer, prostate cancer, lung cancer, colon cancer, rectal cancer, bladder cancer, Non-Hodgkin Lymphoma, melanomas of the skin, cancer of the Kidney and Renal Pelvis, pancreatic cancer, oral cancer, esophagal cancer, ovarian cancer, thyroid cancer, stomach cancer, brain cancer, multiple myeloma, liver and intrahepatic bile duct cancer, acute myeloid leukemia, chronic lymphocytic leukemia, Hodgkin's Lymphoma, testicular cancer, intestinal cancer, chronic myeloid leukemia, acute lymphocytic leukemia, cancer of the vulva, gallbladder cancer, malignant mesothelioma, bone cancer, joint cancer, cancer of the hypopharynx, cancer of the eye, cancer of the nose, cancer of the ureter, cancer of the peritoneum, gastrointestinal carcinoid tumors, bladder cancer, melanoma, breast cancer, non-hodgkin's lymphoma, ovarian cancer, endometrial cancer, pancreatic cancer, kidney cancer (renal cell), prostate cancer, leukemia, non-melanoma cancer of the skin. Also included are sarcomas and carcinomas, such as the following: fibrosarcoma, myxosarcoma, liposarcoma, chondrosarcoma, osteogenic sarcoma, chordoma, angiosarcoma, endotheliosarcoma, lymphangiosarcoma, lymphangio-endotheliosarcoma, synovioma, mesothelioma, ewing's tumor, leiomyosarcoma, rhabdomyosarcoma, colon carcinoma, pancreatic cancer, ovarian cancer, prostate cancer, squamous cell carcinoma, basal cell carcinoma, adenocarcinoma, sweat gland carcinoma, sebaceous gland carcinoma, papillary carcinoma, papillary adenocarcinoma, cystadenocarcinoma, medullary carcinoma, bronchogenic carcinoma, renal cell carcinoma, hepatoma, bile duct carcinoma, choriocarcinoma, seminoma, embryonal carcinoma, Wilms' tumor, cervical cancer, testicular tumor, lung carcinoma, small cell lung carcinoma, bladder carcinoma, epithelial carcinoma, glioma, astrocytoma, medulloblastoma, craniopharyngioma, ependymoma, pinealoma, hemangioblastoma, acoustic neuroma, oligodendroglioma, meningioma, melanoma, neuroblastoma, retinoblastoma, leukemia, lymphoma, multiple myeloma, Waldenströom's macroglobulinemia, and heavy chain disease.

The following references discuss the matter of various attempts by oncologists to treat cancer: Viallet (*Lung Cancer* 15 (3) 367-73, 1996); Kemeny (*Seminars in Oncology* 21 (4 Suppl 7) 67-75, 1994); Newton (*Expert Opinion on Investigational Drugs* 9 (12) 2815-29, 2000); Giese (*Journal of Cancer Research and Clinical Oncology* 127 (4) 217-25, 2001); Garattini (*European Journal of Cancer* 37 Suppl 8 S128-47, 2001); Ragnhammar (*Acta Oncologica* 40 (2-3) 282-308, 2001). As is evident, attempts to treat cancer frequently lead to "unpredictable" outcomes.

It is noted that applicants have obtained some data, and presented this in a graph, which has been labeled as "figure 9". With respect to this, applicants have asserted that some sort of tumor may have been implanted into a mouse. However, the tumor that was used has not been identified. It may be the case that applicants do not know which tumor was used, or indeed if it was a tumor at all. Accordingly, applicants results as present in figure 9 are highly suspect, and no conclusions can be drawn therefrom.

Perhaps it will turn out, at some point in the future, that applicants will assert that some sort of prostate tumor cells were implanted in the mouse. If so, the question will arise as to which other form(s) of cancer can be successfully treated. In reality, extrapolation from treatment of one form of cancer to other forms of cancer leads to "unpredictable" results. In traversing the foregoing assertion, applicants are requested to provide a few examples of chemical agents that are

effective to treat all forms of cancer. This will form the basis for further discussion.

There is another matter, which is that applicants are extrapolating from results obtained with testosterone to a therapy proposed for any other steroid. As disclosed in Kampa, Marilena (*Experimental Cell Research* **307**(1), 41-51, 2005), activation of estrogen receptors results in cytoprotection of T47D cells, whereas activation of androgen receptors results in apoptosis of the same. Thus, in many cases, administration of a steroid/protein conjugate will result in exacerbation of the patient's condition, rather than an amelioration.

In addition, the claims now encompass steroid/protein conjugates in which the protein is obtained from a plant, fungus, bacteria or a reptile. As such, the "window of opportunity" for the conjugates to eradicate the cancer is quite small. Within a matter of days, antibodies will develop to the conjugates, producing an inflammatory reaction which will worsen the patients condition; moreover, the efficacy of the protein conjugates will diminish over time as a result of their antigenicity.

As stated in *Ex parte Forman* (230 USPQ 546, 1986) and *In re Wands* (8 USPQ2d 1400, Fed. Cir., 1988) the factors to consider in evaluating the need (or absence of need) for "undue experimentation" are the following: quantity of experimentation necessary, amount of direction or guidance presented, presence or absence of working examples, nature of the invention, state of the prior art,

relative skill of those in that art, predictability or unpredictability of the art, and breadth of the claims.

Accordingly, "undue experimentation" would be required to practice the claimed invention.

✦

Claims 28-32, 34-47 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 28 recites that the steroid in question is covalently bonded to a protein. The issue here is that throughout the specification, all references to a protein in the conjugate require the protein to be mammalian. Now, the claims encompass plant proteins, fungal proteins, bacterial proteins, viral proteins, and reptilian proteins. For example, ricin/steroid conjugates would be included, whereas they were not before.

Applicants are requested to point to the page and line number where it is suggested that proteins from plants, fungi, bacteria, viruses and/or reptiles are included.

✦

Claim 44 is objected to for each of two reasons: (a) there should be a hyphen, or at least a space between "testosterone" and "3", and (b) the indefinite article should be present between "thereof" and "composition".

✦

Claims 33 and 48 are rejected under 35 U.S.C. §112 second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

- In claim 33, the phrase "the mammalian protein" lacks antecedent basis.
- Claim 48 characterizes a "binder" as a mammalian protein. Applicants are requested to provide a specific example of a mammalian protein that they believe would qualify as a binder.

✦

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Lukton whose telephone number is 571-272-0952. The examiner can normally be reached Monday-Friday from 9:30 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang, can be reached at (571)272-0562. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

D. Lukton

DAVID LUKTON, PH.D.
PRIMARY EXAMINER